SECOND DECLARATION FOR BCS 03-3056 US

DECLARATION UNDER 37 CFR 1.132

I, Andreas Guenther, of Kuckelbergweg 3a, 51069 Cologne, Germany, declare as follows:

1. I studied at the University of Hannover, Germany, where I obtained a degree of doctor rer. nat. in chemistry. Since September 1, 1980, I have been employed by Bayer AG, Leverkusen, Germany, and remain employed in the process department IOP-IND with Bayer CropScience AG in Dormagen, Germany. I specialize in the field of process chemistry.

2. I am an inventor of, and I am familiar with the subject matter disclosed in the present United States patent application no. 10/588,355 ("the '355 application").

3. I have reviewed WO 02/16304 to Müh *et al.* ("the Müh reference") which has been cited against the claims of the '355 application.

4. Attached herewith as Exhibits A, B and C are true and accurate English language translations of business records prepared and maintained in the ordinary course of business of a laboratory of Bayer AG, Leverkusen, Germany. A copy of each record in the German language as originally prepared is appended to its respective English language translation. I have reviewed the records of Exhibits A, B and C in making this Declaration.

5. Exhibit A is a record dated May 23, 2000, of a protocol of an experiment carried out under the supervision of Dr. Müh that corresponds to Example 1 described in the Müh reference. As provided in the experiment of Exhibit A, the reaction yielded approximately 86% of fluoromalonic ester product using 3 equivalents of reactants (triethylamine and hydrogen fluoride) per equivalent diethyl chloromalonate. In particular, 494 g of triethylamine bishydrofluoride and 357 g triethylamine were heated to 105°C, and 535 g of diethyl chloromalonate was metered in over 6 hours. The reaction mixture was stirred at 105°C, and the reaction time was 12 hours at an inherent pressure of just under 6 bar.

6. Accordingly, the experiment of Exhibit A shows that, under the method described in Example 1 of the Müh reference, for the documented reaction

temperature of about 105°C and the reaction time of 12 hours, the reaction pressure was just under 6 bar.

7. Exhibit B is a record dated July 21, 2000, of a general description of the method used in the Examples 1 and 2 of the Müh reference, this general description differing from the Examples of the Müh reference in the amounts of the reagents used. The general description indicates that the pressure-resistant reaction vessel was sealed so as to be pressure-sealed after adding the reagents of triethylamine and hydrogen fluoride into the vessel, and then the contents of triethylamine and hydrogen fluoride were heated to 105°C. Diethyl chloromalonate was metered in within 6 hours and the mixture was stirred for an additional 6 hours at 105°C. Accordingly, the reaction time in the pressure-resistant reaction vessel at 105°C was 12 hours. The general description of the method provided by the Exhibit B record was used to carry out the experiment of Exhibit A and the experiment of Exhibit C, described below.

8. Exhibit C is a record dated October 30, 2000, of an internal order for an experiment carried out on behalf of Dr. Pleschke. This experiment corresponds to Example 2 described in the Müh reference in which 2 equivalents of reactants (triethylamine and hydrogen fluoride) per equivalent diethyl chloromalonate are used. The internal order includes a two page attachment of time, temperature and pressure data monitored during the experiment.

9. As provided in the experiment of Exhibit C, the reaction was conducted in a 3 liter autoclave, in which the reactants were heated to 105°C. When the metering of the chloromalonic ester was started (at time 14:30), the documented operating temperature and pressure were 102°C and 3.5 bar. When the metering was stopped about 6 hours later (at time 20:25), the operating temperature and pressure were 105°C and 5.6 bar. After an additional reaction time of 6 hours (at time 2:25), the documented operating temperature and pressure were 104.7°C and 6.9 bar.

10. Accordingly, the experiment of Exhibit C shows that, under the method described in Example 2 of the Müh reference, for the documented reaction temperature of about 105°C and the reaction time of 12 hours, the reaction pressure ranged from 3.5 bar to 6.9 bar.

11. In comparison to the experiments of Exhibits A and C, Example 1 of the '355 application shows that for the reaction temperature of 105 to 110°C under normal pressure (800 to 1200 mbar), the reaction time is 15 hours.

12. Thus, the method of the Müh reference requires a reaction pressure about 5 times higher than that of the '355 application in order to achieve a comparable short reaction time of 12 hours.

13. In my opinion, one of skill in the art, attempting to achieve a short reaction time for preparing dialkyl alpha-fluoromalonates, would not have been led by the teachings of the Müh reference to reduce the pressure to normal pressure since the method of Müh reference clearly requires the reaction to be conducted under increased pressure, and further requires such increased pressure to be significantly higher than normal pressure, at almost 6 bar and higher, to achieve the short reaction time of 12 hours.

14. In addition, U.S. Patent No. 5,391,811 to Bohm *et al.* ("Bohm"), discussed in the Declaration under 37 CFR 1.132 executed by me on December 22, 2008, describes a method carried out under normal pressure in which the reaction time is 72 hours. In light of the long reaction time described in the Bohm reference, in my opinion, one of skill in the art would not have been led to reduce the pressure of the method of the Müh reference to normal pressure to achieve a short reaction time.

6. The undersigned declares further that all statements made herein of his own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing therefrom.

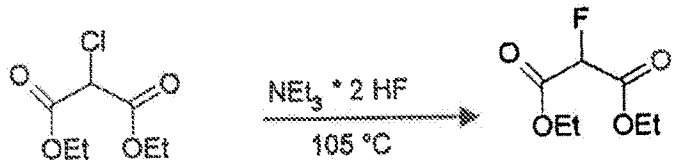
Signed at Dormagen, this 2nd day of June, 2010.

Andreas Guenther

Exhibit A

Project:	HEC 5725	**Date of test:**	**23.05.00**
Stage/procedure variant:	**Fluoromalonic ester**	**Carried out by:**	**Muscara**
Test No.: MUEH 9/34		**Head of laboratory:**	**Dr Müh**
Note:			

Reaction equation:



Diethyl chloromalonate
194.5 g/mol

Diethyl fluoromalonate
178 g/mol

Starting materials

Weight (g)	(mol)	Purity (%)	
535	2.33	84.7	Diethyl chloromalonate MUEH 14/25 (3.2% diethyl malonate, 15.2% diethyl dichloromalonate)
494	3.5	100	Triethylamine bishydrofluoride (Fluorlabor)(0.18% water)
357	3.5	99	Triethylamine (Riedel de Haen)

Description of the test

Introduce triethylamine bishydrofluoride and triethylamine, heat to 105°C, then meter in diethyl chloromalonate over 6 h.

Continue stirring the mixture at 105°C until measurements show that the development of heat has ceased.

The reaction time under an inherent pressure of just under 6 bar was 12 hours.

After the reaction has ended, the mixture is cooled to RT, and 494.5 g of water are added to dissolve the suspension. Record the amount of reaction mixture removed for further DTA tests.

1618 g of final reaction mixture were worked up with 12 g of crystal complexes (which are soluble in 50 g of water).

After phase separation, 525 g of organic and 1093 g of aqueous phase are obtained; the latter does not contain any product.

Yield: approximately 85% of product

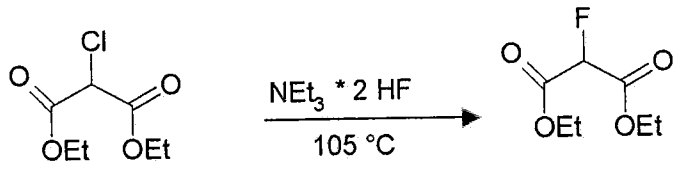
m = 525 g GC_{ISTD} = 67.2%

Test A as described in WO 02/16304 (Müh)

Projekt:	**HEC 5725**	**Versuchsdatum:**	**23.05.00**
Stufe/Verfahrensvariante:	**Fluormalonester**	**Durchführende :**	**Muscara**
Versuchs-Nr.:	**MUEH 9/34**	**Laborleiter:**	**Dr. Müh**

Bemerkung :

Reaktionsgleichung:



Chlormalonsäure-diethylester
194,5 g / mol

Fluormalonsäure-diethylester
178 g / mol

Einsatzstoffe

Masse (g)	(mol)	Gehalt (%)	
535	2,33	84,7	Chlormalonsäurediethylester MUEH 14/25 (3,2 %Malonsäurediethylester, 15,2 % Dichlormalonsäurediethylester)
494	3,5	100	Triethylamin-Bishydrofluorid (Fluorlabor)(0,18 % Wasser)
357	3,5	99	Triethylamin (Riedel de Haen)

Versuchsbeschreibung

Das Triethylamin-Bishydrofluorid und Triethylamin vorlgen und auf 105°C aufheizen, anschließend in 6 h den Chlormalonsäurediethylester zudosieren.
Den Ansatz solange bei 105 °C nachrühren, bis keine Wärmeentwicklung mehr gemessen wird.
Die Reaktionszeit unter einem Eigendruck von knapp 6 bar betrug 12 Stunden.
Nach Reaktionsende wird der Ansatz auf RT abgekühlt und es werden 494,5 g Wasser zugeben, um die Suspension zu lösen. Die abgenommene Menge an Reaktionsgemisch für weitere DTA-Versuche protokollieren.

1618 g Reaktionsendgemisch mit 12 g (in 50 g Wasser löslichen) Kristallkomplexen wurde aufgearbeitet.
Nach der Phasentrennung erhielt man 525 g organische und 1093 g wäßrige Phase, wobei letztere kein Produkt enthielt.

Ausbeute: ca. 85% Produkt

$m = 525$ g $GC_{ISTD} = 67{,}2$ %

Versuch A gemäß WO 02/16304 (Müh)

Exhibit B

General description of the reaction Test "A" & "B" Bayer

Müh

PF-P+T VE
21 July 2000
Leverkusen B 202

Example for the fluorination of diethyl chloromalonate to give diethyl fluoromalonate

Into a pressure-resistant reaction vessel there are introduced 453 g of the adduct (3.21 mol) of 3.21 mol of triethylamine and 6.42 mol of hydrogen fluoride and a further 325 g of triethylamine (3.21 mol). The reaction vessel was sealed so as to be pressure-sealed and the contents were heated to 105°C. Within 6 hours, 541 g of diethyl chloromalonate (purity 77%; 2.14 mol) were metered in via a pump at 105°C, and the mixture was then stirred for a further 6 h at 105°C until the reaction was complete. After the reaction had ended, the mixture was cooled to 40°C, and 750 g of water were added in order to completely dissolve the suspension which was present after the reaction had ended. The organic bottom phase (440 g) was washed with 150 g of 15% strength sulphuric acid. This gave 420 g of a dark liquid which contains 73% of diethyl fluoromalonate (yield: approximately 81%), which was used in the next step partly directly and partly after distillation.

Bayer

Müh

PF-P+T VE
21. Juli 2000
Leverkusen B 202

Beispiel für die Fluorierung von Chlormalonsäurediethylester zu Fluormalonsäurediethylester

In einem druckfesten Reaktionsbehälter werden 453 g des Additionsproduktes (3,21 Mol) von 3,21 Mol Triethylamin mit 6,42 Mol Fluorwasserstoff vorgelegt und mit weiteren 325 g Triethylamin (3,21 Mol) versetzt. Der Reaktionsbehälter wurde druckdicht verschlossen und der Behälterinhalt auf 105 °C aufgeheizt. Innerhalb von 6 h wurden 541 g Chlormalonsäurediethylester (Reinheit 77 %; 2,14 Mol) bei 105 °C über eine Pumpe zudosiert und anschließend weitere 6 h bei 105 °C bis zum vollständigen Umsatz gerührt. Nach Reaktionsende wurde auf 40 °C abgekühlt und 750 g Wasser zugegeben, um die nach Reaktionsende vorliegende Suspension vollständig aufzulösen. Die untere, organische Phase (440 g) wurde mit 150 g 15 % iger Schwefelsäure gewaschen. Man erhält 420 g einer dunklen Flüssigkeit, die 73 % Fluormalonsäurediethylester enthält (Ausbeute: ca. 81 %), der teilweise direkt, teilweise nach Destillation für die nächste Stufe verwendet wurde.

Exhibit C

Test "B" as specified in WO 02/16304 (Müh)

Test as described by Müh

Operating instructions

Bayer

HD Laboratory Q 17
ZF-SFO 1
Leverkusen

Box/ Chamber: L4

Q17 No.: QI 1454

Commissioned by: Dr. Pleiß

Dept./Acct.: 2F-5FF

J. No.:

Tel.:

Carried out by:

Autoclave: 5 l IC

Reaction conditions

(filled in by the HD Laboratory):

Time: Hours

Temp.: see protocol

Pressure: bar

Heat at a rate of: bar

Run at: bar

Uptake (calc.): bar

Cl. No.:

Assembly:

Speed: rpm

GC sample(s):

Test B as specified in WO 02/16304 (Müh)

Starting materials:

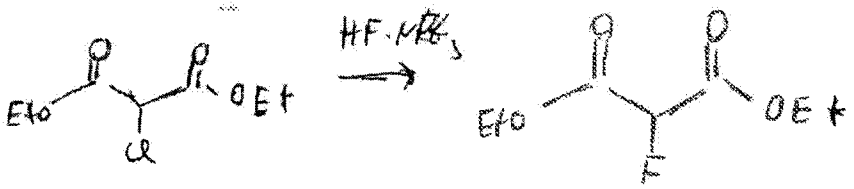
Quantity (g/ml)	Designation (if appropriate manufacturer, purity, other specifications)	MW	eq.
	See protocol		

Risk statements (tick where applicable, if appropriate add risk phrases)

☒ poisonous	☐ explosive	☐ irritating	Other properties/statements:
☐ may cause cancer	☐ flammable	☐ substance not fully tested	
☐ mutagenic	☐ causes burns		

Safety phrases:

Reaction equation/procedure:



Test results (on enclosed copy, back to Q17):

Conversion rate:	Other:
Yield:	
Date: 30.10.00	Signature:

0027 BAQ - 518 b

Copy for client

Bayer
ZF - FGF
HD Laboratory Q 17
Leverkusen

No. 00 - 1434

Chamber / Box 24

Leverkusen, 06.11.2000

for Dr Plesch/Ke

Telephone

Test No.

Autoclave: 14864 ; litres: 3

Mat.: HC

bar: 300 ; Temp.: 300 °C

Time		Temperature external	Temperature internal	Heating	Pressure in bar measured	Pressure in bar injected	Pressure in bar diff.	N2	M
Introduce triethylamine					flushed with N_2				
									HF
10	40		62		0.7	5 g	to [illegible] +		10 g
	43		61		1.4				
	58		61		1.5			+	10 g
11	13		65		1.9			+	10 g
	22		59		1.4			+	10 g
	34		63		1.9			+	10 g
	58		62		2			+	10 g
12	13		59		1.9			+	10 g
	28		61		1.8			+	10 g
	43		61		1.7			+	10 g
	57		60		1.7			+	10 g
13	13		62		1.7			+	10 g
		Internal to			105 °C				
~ 80 mL/h	14	30	102		3.5	Start metering in (ester)			
	15	30	104.5		3.8				

Pressure drop calc.: ____ found: ____

0027835 - 995

Time		Temperature		Heating	Pressure in bar			
		external	internal		measured	injected	diff.	
16	20		104.7		4.06			
17	15		104.5		4.28			
18	20		104.8		4.61			
19	30		105.0		5.00			
20	5		105.0		5.6	Stop pumping		
21	25		104.7		5.84			
22	25		104.7		6.06			
23	25		104.7		6.31			
0	25		104.7		6.64			
1	25		104.7		6.69			
2	25		104.7		6.90	Cooling to 40°C		
4	10		40.5		4.15	Start pumping deionized H_2O		
	35		41.1		4.20			
5	10		38.9		4.53			
	20		37.1		4.75	Stop pumping deionized H_2O		

Cooling to RT

Rinse autoclave with 150 g of deionized water

Betriebsanweisung

Bayer

HD-Labor Q 17
ZF-SFO 1
Leverkusen

Boxe/ Kammer: L4

Q17-Nr.: Q 1454

Auftraggeber: Dr. Pleschke

J.-Nr.:

Bearbeiter:

Abt./Klo.: ZF-SFF

Tel.:

Autoklav:

Reaktionsbedingungen: (wird im HD-Labor ausgefüllt)

Kl.-Nr.:

Zeit: Std.

aufheizen mit: bar

Bestückung:

Temp.: s.d. Vorschrift

fahren mit: bar

Drehzahl: UpM

Druck: bar

Aufnahme (ber.): bar

GC-Probe(n):

Einsatzstoffe:

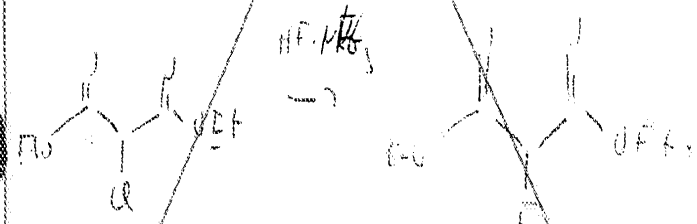
Menge (g/ml)	Bezeichnung (ggf. Hersteller, Reinheit, sonstige Spezifikationen)	MG	Mol
	s.d. Vorschrift		

Gefahrenhinweise (zutreffendes ankreuzen, ggf. mit R-Sätzen ergänzen):

☐ giftig	☐ explosionsgef.	☐ reizend	Sonstige Eigenschaften/Hinweise:
☐ krebserr.	☐ entzündl.	☐ nicht vollständig gepr. Stoff	
☐ erbgutveränd.	☐ ätzend		

SI-Ratschläge (S-Sätze):

Reaktionsgleichung/Durchführung:



Versuchsergebnisse (auf beiliegender Kopie zurück an Q17):

Umsatz: Sonstiges:

Ausbeute:

Datum: 3.11.00 Unterschrift:

0027 843 - 918 c

Mit Ergebnis zurück an das HD-Labor Q17

Betriebsanweisung

Bayer

HD-Labor Q 17
ZF-SFO 1
Leverkusen

Boxe/ Kammer: L4

Q17-Nr.: Q 1454

Auftraggeber: Dr. Pleschke

J.-Nr.:

Bearbeiter:

Abt./Klo.: ZF-SFF

Tel.:

Autoklav:

Reaktionsbedingungen: (wird im HD-Labor ausgefüllt)

Kl.-Nr.:

Zeit: Std.

aufheizen mit: bar

Bestückung:

Temp.: s.d. Vorschrift

fahren mit: bar

Drehzahl: U

Druck: bar

Aufnahme (ber.): bar

GC-Probe(n):

Einsatzstoffe:

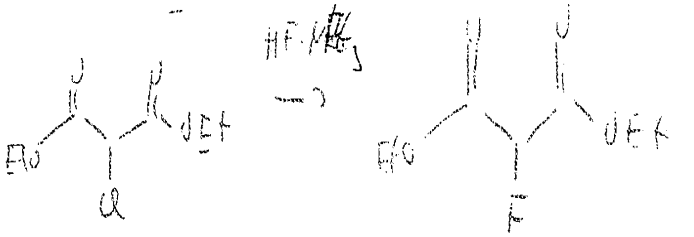
Menge (g/ml)	Bezeichnung (ggf. Hersteller, Reinheit, sonstige Spezifikationen)	MG
	s.d. Vorschrift	

Gefahrenhinweise (zutreffendes ankreuzen, ggf. mit R-Sätzen ergänzen):

☐ giftig	☐ explosionsgef.	☐ reizend	Sonstige Eigenschaften/Hinweise:
☐ krebserr.	☐ entzündl.	☐ nicht vollständig gepr. Stoff	
☐ erbgutveränd.	☐ ätzend		

SI-Ratschläge (S-Sätze):

Reaktionsgleichung/Durchführung:



Versuchsergebnisse (auf beiliegender Kopie zurück an Q17):

Umsatz: Sonstiges:

Ausbeute:

Datum: 3.11.00 Unterschrift:

0027 843 - 918 b

Kopie für Auftraggeber

HD - Labor Q 17
Leverkusen

Kammer / Boxe C4

Leverkusen, den 06.11.2000

für Dr. Pleschke

Telefon

Vers. Nr.

Autoklav: 14864 ; Ltr.: 3

Mat.: HC

bar: 300 ; Temp.: 300 °C

Zeit		Temperatur außen	Temperatur innen	Hzg.	Druck in bar gem.	Druck in bar aufgedr.	Druck in bar Diff.	ΔR	N_2
Triethylamin			ungeeegt		N_2 gegen				HF
10	40		62		0,7	5g	bis Verd.	+	10 g
	43		61		1,4				
	58		61		1,5			+	10 g
11	12		65		1,9			+	10 g
	28		59		1,4			+	10 g
	44		63		1,9			+	10 g
	58		62		2			+	10 g
12	12		59		1,9			+	10 g
	28		61		1,8			+	10 g
	43		61		1,7			+	10 g
	57		60		1,7			+	10 g
13	13		62		1,7			+	10 g
	Innen		auf		105 °C				
280ml/h	14 20		102		3,5	Beg	mit Wasser	(ester)	
	15 20		104,5		3,8				

Druckabfall ber.: ..... gef.: .....

		außen	innen		gem.	aufgedr.	Diff.		
16	20		104,7		4,06				
17	15		104,5		4,28				
18	20		104,8		4,61				
19	30		105,0		5,00				
20	15		105.0		5,6	Ende d. Pumpe			
21	25		104,7		5,84				
22	25		104,7		6,06				
23	35		104,2		6,31				
0	15		104,7		6,64				
1	25		104,7		6,69				
2	25		104,7		6,90	Kreislauf auf 10°C			
4	10		40,5		4,15	Beg. mit Pumpe E-40			
	35		41,1		4,20				
5	10		38,9		4,53				
	20		39,1		4,75	Ende mit Pumpe E-40			
	Abkühlen auf RT,								
		Zutaten		mit	1150g	E-Wasser	ausgep		